UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/972,799	10/05/2001	Mohler Hanns	9261-005	5224

20583 7590 11/20/2003

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
LANDSMAN, ROBERT S	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 11/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

KC

Office Action Summary	Application No.	Applicant(s)	
	09/972,799	HANNS ET AL.	
	Examin r	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *2-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 19-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ *Claim(s) _____ are subject to restriction and/or election requirement.*

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9/8/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Claims 1-18 were pending in this Office Action. In the Amendment filed 9/8/03, Applicants elected Group I and added claim 19-21. Therefore, claims 1-21 are pending and claims 1 and 19-21 are the subject of this Office Action.

B. The Information Disclosure Statement, filed 9/8/03, has been entered into the record.

2. Title

A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The claims of the present invention are drawn to methods for screening ligands.

3. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 1 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of demonstrating that α2-$GABA_A$ receptor knockout mice do not show anxiolytic effects when administered benzodiazepine, does not reasonably provide enablement for the claimed screening methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the only guidance and working examples that Applicants have provided is that mice with the α2-$GABA_A$ receptor knockout do not respond to the anxiolytic effects of benzodiazepine. None of the Figures presented in the specification provide any support for the claimed invention. Support of the claims by the Figures is not required for enablement, but the Examiner just wanted to clarify the fact that the only support for the anxiolytic effect of benzodiazepine as acting through the α2-$GABA_A$ receptor is the discussion on page 26, starting on line 24 of the disclosure. No information has been provided on the effect of the α1-$GABA_A$ receptor or the α5-$GABA_A$ receptor on anxiety, nor have Applicants identified any compounds which selectively bind to the α2-$GABA_A$ receptor to reduce anxiety. Furthermore, it is not predictable to the artisan what the effects of knocking out the α1-$GABA_A$ receptor or the α5-$GABA_A$ receptor genes would be on anxiety, nor would it be predictable that the only requirement for anxiolytic effects is to find compounds which selectively bind to the α2-$GABA_A$ receptor, or, as seen in claims 19-21, what the effects of ligands activating α3-$GABA_A$ receptor or the α5-$GABA_A$ receptor would be. If any pertinent information is provided in the specification, it is respectfully requested that Applicants point out exactly where in the specification this information can be found. As stands, Applicants are only enabled for demonstrating that α2-$GABA_A$ receptor knockout mice do not respond to the anxiolytic effects of benzodiazepine.

Therefore, the breadth of the claims is excessive since Applicants have not provided any guidance or working examples of α2-$GABA_A$ receptor-selective compounds which are anxiolytic, nor for screening methods which can identify anxiolytic compounds by comparing their α2-$GABA_A$ receptor-binding ability to their ability to bind the α1-$GABA_A$ receptor, α3-$GABA_A$ receptor, or the α5-$GABA_A$ receptor. Furthermore, it is not predictable to the artisan that the only requirement for anxiolytic effects is to find compounds which selectively bind to the α2-$GABA_A$ receptor. Therefore, the Examiner has concluded that undue experimentation would be required to practice the invention as claimed.

4. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 1 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Applicants have not identified any compounds which selectively bind the α2-GABA$_A$ receptor to reduce anxiety. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus, other than that they must bind the α2-GABA$_A$ receptor. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the chemical class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "compounds which selectively bind to the α2-GABA$_A$ receptor to produce anxiolytic effects" alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

5. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 1 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are confusing since it is not clear in claim 1 how a compound which simply "binds" to the α2-GABA$_A$ receptor would have anxiolytic effects. This would include compounds which bind but do not "activate" the receptor. Therefore, if a compound binds to, but does not activate the receptor, it is no understood how this compound would be anxiolytic.

B. Claims 19-21 are confusing since it is not clear how Applicants have concluded that any effect on the α5-GABA$_A$ receptor would have no effect on the claimed anxiolytic properties. The specification is not clear as to what role the α5-GABA$_A$ receptor plays in anxiety.

6. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 1 and 19-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Ladduwahetty et al. (US Patent 6,444,666). The claims recite methods of identifying anxiolytic compounds by identifying those which are selective for the α2-GABA$_A$ receptor. Ladduwahetty teach that compounds which selectively bind the α2-GABA$_A$ receptor subunit as compared to the α2-GABA$_A$ receptor subunit will be anxiolytic (column 2, lines 10-26 and column 2, line 60 – column 3, line 46). It can also be seen in these passages that the α5-GABA$_A$ receptor subunit appears to have no effect on anxiety, and is responsible for cognition. Though it appears that the reference is silent to the use of screening methods, the artisan would immediately envision these methods. In fact, it is inherent in the identification of the compounds of the patent that screening methods must be employed in order to determine the selectivity of the produced compounds.

B. Claims 1 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Rudolph et al. (Nature 401:796-800, 1999). The claims recite methods of identifying anxiolytic compounds by identifying those which are selective for the α2-GABA$_A$ receptor. Rudolph teach that the anxiolytic compounds likely act via the α2-GABA$_A$ receptor, the α3-GABA$_A$ receptor, or the α5-GABA$_A$ receptor and not the α1-GABA$_A$ receptor. Rudolph et al. teach the use of screening methods using H101R mice (page 799, especially the first full paragraph on the right column). Though it appears that the reference is silent to the specifically claimed screening methods, the artisan would immediately envision these methods. In fact, it is inherent in the

identification of the compounds of the patent that screening methods must be employed in order to determine the selectivity of the produced compounds. In fact, Rudolph do teach numerous screening assays (Figures 2-4).

7. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 1 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ladduwahetty et al. (US Patent 6,444,666). The claims recite methods of identifying anxiolytic compounds by identifying those which are selective for the α2-GABA$_A$ receptor. Ladduwahetty teach that compounds which selectively bind the α2-GABA$_A$ receptor subunit as compared to the α2-GABA$_A$ receptor subunit will be anxiolytic (column 2, lines 10-26 and column 2, line 60 – column 3, line 46). It can also be seen in these passages that the α5-GABA$_A$ receptor subunit appears to have no effect on anxiety, and is responsible for cognition. Though it appears that the reference is silent to the use of screening methods, it would have been obvious to the artisan at the time of the present invention to have used a screening method in order to identify compounds which selectively bind to the α2-GABA$_A$ receptor. The artisan would have been motivated to have performed these screening methods in order to draw the desired conclusion that the developed compounds do, in fact, bind to the desired subunit to produce the desired effects.

B. Claims 1 and 19-21 are rejected under 35 U.S.C. 103(ab) as being unpatentable over Rudolph et al. (Nature 401:796-800, 1999). The claims recite methods of identifying anxiolytic compounds by identifying those which are selective for the α2-GABA$_A$ receptor. Rudolph teach that the anxiolytic compounds likely act via the α2-GABA$_A$ receptor, the α3-GABA$_A$ receptor, or the α5-GABA$_A$ receptor and not the α1-GABA$_A$ receptor. Rudolph et al. teach the use of screening methods using H101R mice (page 799, especially the first full paragraph on the right column). Though it appears that the reference is silent to the specifically claimed screening methods, it would have been obvious to the artisan at the time of the present invention to have

used a screening method in order to identify compounds which selectively bind to the α2-$GABA_A$ receptor. The artisan would have been motivated to have performed these screening methods in order to draw the desired conclusion that the developed compounds do, in fact, bind to the desired subunit to produce the desired effects.

8. Art of Interest

A. McKernan et al. (Nature Neuroscience 3 (6) :587-592, 1999 is being cited to further demonstrate that it was known in the art at the time of the present invention that the α1-$GABA_A$ receptor did not mediate anxiety.

9. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
November 14, 2003

ROBERT LANDSMAN
PATENT EXAMINER